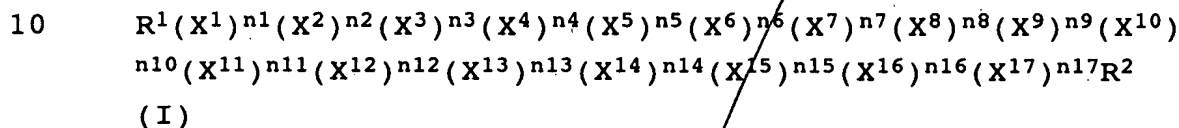


# CLAIMS

1. A peptide having a cyclic structure and having an activity to restore the DNA-binding activity or the P53 protein-dependent transcription activity to mutant P53 protein, or a pharmaceutically acceptable salt thereof, said peptide being represented by general formula (I):



{wherein any of  $X^1$  to  $X^{17}$  and  $n_1$  to  $n_{17}$  may be denoted by  $X^i$  and  $n_i$ , respectively ( $i$  stands for an integer of 1 to 17);  $X^i$  represents an amino acid residue or an organic acid residue as defined below;  $n_i$  represents 0 or 1;  $(X^i)^{n_i}$  represents  $X^i$  when  $n_i$  is 1, and represents a bond when  $n_i$  is 0; 7 to 17 different  $X^i$ s ( $n_i=1$ ) are selected, arranged in order of increasing number  $i$ , and bonded to one another, with  $R^1$  bonded to the N-terminus and  $R^2$  bonded to the C-terminus, to represent one sequence, in which a functional group in residue  $X^p$  ( $p$  is an integer of 1 to 11) is selected from the group of  $X^1$  to  $X^{11}$  and a functional group in residue  $X^q$  ( $q$  is an integer of 8 to 17, provided that  $q$  is larger than  $p$ ) is selected from the group of  $X^8$  to  $X^{17}$  form a cyclic structure;  $R^1$  represents substituted or unsubstituted alkanoyl, substituted or unsubstituted alkoxy carbonyl, substituted or unsubstituted aralkyloxy carbonyl, substituted or unsubstituted aryloxy carbonyl, substituted or unsubstituted aroyl, 9-fluorenylmethoxycarbonyl, or hydrogen;  $X^1$  represents a residue of 2-mercaptobenzoic acid, 3-mercaptopropionic acid, 4-mercaptobutanoic acid, mercaptoacetic acid, adipic acid, suberic acid, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid, 2-aminosuberic

acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, serine, threonine, homoserine,  $\alpha$ -methylserine, 3-hydroxyproline or 4-hydroxyproline;  $X^2$  represents a residue of leucine,

5 isoleucine, valine, alanine, norvaline, norleucine, 2-aminobutanoic acid, homoleucine,  $\beta$ -alanine,  $\alpha$ -aminoisobutanoic acid,  $\beta$ -cyclopropylalanine,  $\beta$ -chloroalanine, 1-aminocyclopentane-1-carboxylic acid, 1-amino-1-cyclohexanecarboxylic acid, 2-amino-1-

10 cyclopentanecarboxylic acid, t-butylglycine, diethylglycine, t-butylalanine, O-methylserine, cyclohexylglycine, cyclohexylalanine or glycine;  $X^3$  represents a residue of lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-

15 aminophenylalanine or glycine;  $X^4$  represents a residue of serine, threonine, homoserine,  $\alpha$ -methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid,

20 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptobenzoic acid, 3-mercaptopropionic acid, 4-mercaptobutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;  $X^5$  represents a residue of lysine, arginine,

25 ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;  $X^6$  represents a residue of lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;  $X^7$  represents a residue of alanine,  $\beta$ -alanine, 2-aminobenzoic

30 acid, 3-aminobenzoic acid, 4-aminobenzoic acid, 3-aminomethylbenzoic acid, proline, 3-hydroxyproline, 4-hydroxyproline, L-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid, cysteine, homocysteine, penicillamine, 2,3-diaminopropionic acid, 2,4-diaminobutanoic acid,

35 ornithine, lysine, p-aminophenylalanine, aspartic acid, glutamic acid, isoaspartic acid, isoglutamic acid, 2-

aminoadipic acid, 2-aminosuberic acid or glycine;  $X^8$  represents a residue of glutamine, asparagine, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-  
 5 aminoadipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, serine, threonine, homoserine,  $\alpha$ -methylserine, 3-hydroxyproline, 4-hydroxyproline, glycine, 2-mercaptobenzoic acid, 3-mercaptopropionic acid, 4-  
 10 mercaptobutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;  $X^9$  represents a residue of serine, threonine, homoserine,  $\alpha$ -methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic  
 15 acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptobenzoic acid, 3-mercaptopropionic acid, 4-mercaptobutanoic acid, mercaptoacetic acid, adipic acid or  
 20 suberic acid;  $X^{10}$  represents a residue of serine, threonine, homoserine,  $\alpha$ -methylserine, hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid, ornithine, lysine,  
 25 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptobenzoic acid, 3-mercaptopropionic acid, 4-mercaptobutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;  $X^{11}$  represents a residue of serine, threonine, homoserine,  $\alpha$ -  
 30 methylserine, hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine,  
 35 glycine, 2-mercaptobenzoic acid, 3-mercaptopropionic acid, 4-mercaptobutanoic acid, mercaptoacetic acid, adipic acid or

suberic acid;  $X^{12}$  represents a residue of lysine, arginine,  
 ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic  
 acid, p-aminophenylalanine or glycine;  $X^{13}$  represents a  
 residue of histidine, alanine, 4-thiazolylalanine, 2-  
 5 thienylalanine, 2-pyridylalanine, 3-pyridylalanine, 4-  
 pyridylalanine, (3-N-methyl)piperidylalanine, 3-(2-  
 quinoyl)alanine, serine, threonine, homoserine,  $\alpha$ -  
 methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine,  
 homocysteine, penicillamine, aspartic acid, glutamic acid,  
 10 homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-  
 aminoadipic acid, 2-aminosuberic acid, ornithine, lysine,  
 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-  
 aminophenylalanine or glycine;  $X^{14}$  represents a residue of  
 lysine, arginine, ornithine, 2,4-diaminobutanoic acid,  
 15 2,3-diaminopropionic acid, p-aminophenylalanine, serine,  
 threonine, homoserine,  $\alpha$ -methylserine, 3-hydroxyproline,  
 4-hydroxyproline, cysteine, homocysteine, penicillamine,  
 aspartic acid, glutamic acid, homoglutamic acid, isoaspartic  
 acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic  
 20 acid or glycine, and an amino group or guanidino group in the  
 side chain of  $X^{14}$  may be modified with  $R^3$  ( $R^3$  has the same  
 significance as  $R^1$ );  $X^{15}$  represents lysine, arginine,  
 ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic  
 acid, p-aminophenylalanine or glycine;  $X^{16}$  represents a  
 25 residue of leucine, alanine, 4-thiazolylalanine, 2-  
 thienylalanine, isoleucine, norleucine, homoleucine, valine,  
 norvaline,  $\beta$ -alanine,  $\alpha$ -aminoisobutanoic acid, 2-  
 aminobutanoic acid,  $\beta$ -cyclopropylalanine,  $\beta$ -chloroalanine,  
 1-aminocyclopentane-1-carboxylic acid, 1-amino-1-  
 30 cyclohexanecarboxylic acid, 2-amino-1-  
 cyclopentanecarboxylic acid, t-butylglycine,  
 diethylglycine, t-butylalanine, O-methylserine,  
 cyclohexylglycine, cyclohexylalanine or glycine;  $X^{17}$   
 represents a residue of 2-mercaptoaniline, cysteamine,  
 35 homocysteamine, cysteine, homocysteine, penicillamine,  
 ornithine, lysine, 2,3-diaminopropionic acid, 2,4-

diaminobutanoic acid, p-aminophenylalanine, glutamic acid, aspartic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-aminoadipic acid or 2-aminosuberic acid;  $R^2$  represents substituted or unsubstituted alkoxy, substituted or unsubstituted aralkyloxy, amino, substituted or unsubstituted alkylamino, substituted or unsubstituted dialkylamino, substituted or unsubstituted aralkylamino, substituted or unsubstituted arylamino, or hydroxy; and one to several residues which are the same or different and arbitrarily selected from the group consisting of organic acid residues, amino acid residues and a 12-aminododecanoic acid residue mentioned in the above  $X^i$  representations may be deleted, substituted or added at arbitrary positions in the sequence}.

2. A peptide having a cyclic structure or a pharmaceutically acceptable salt thereof according to claim 1, wherein said cyclic structure is formed by a 3-S, S-CH<sub>2</sub>-S, S-CH<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>-CH<sub>2</sub>-S, S-CH<sub>2</sub>-CO, CO-NH, NH-CO, O-CO or CO-O bond between  $X^p$  and  $X^q$ .

3. A peptide having a cyclic structure or a pharmaceutically acceptable salt thereof according to claim 2, wherein  $X^p$  ( $n_p=1$ ) is an N-terminal residue and  $X^q$  ( $n_q=1$ ) is a C-terminal residue.

4. A peptide having a cyclic structure or a pharmaceutically acceptable salt thereof according to claim 2, wherein  $X^p$  ( $n_p=1$ ) is not an N-terminal residue and  $X^q$  ( $n_q=1$ ) is not a C-terminal residue.

5. A peptide having a cyclic structure or a pharmaceutically acceptable salt thereof according to claim 2, wherein  $X^p$  ( $n_p=1$ ) is not an N-terminal residue and  $X^q$  ( $n_q=1$ ) is a C-terminal residue.

6. A peptide having a cyclic structure or a pharmaceutically acceptable salt thereof according to claim 2, wherein  $X^p$  ( $n_p=1$ ) is an N-terminal residue and  $X^q$  ( $n_q=1$ ) is not a C-terminal residue.

5

7. A peptide having a cyclic structure or a pharmaceutically acceptable salt thereof according to claim 3, wherein  $X^p$  ( $n_p=1$ ) is  $X^1$  and  $X^q$  ( $n_q=1$ ) is  $X^{17}$ .

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8. A peptide having a cyclic structure or a pharmaceutically acceptable salt thereof according to claim 6, wherein  $X^p$  ( $n_p=1$ ) is  $X^1$  and  $X^q$  ( $n_q=1$ ) is  $X^{17}$ .

15

9. A peptide having a cyclic structure or a pharmaceutically acceptable salt thereof according to claim 3, wherein  $X^p$  ( $n_p=1$ ) is  $X^1$  and  $X^q$  ( $n_q=1$ ) is  $X^{16}$ .

20

10. A peptide having a cyclic structure or a pharmaceutically acceptable salt thereof according to claim 6, wherein  $X^p$  ( $n_p=1$ ) is an N-terminal residue and  $X^q$  ( $n_q=1$ ) is  $X^8$ .

25

11. A peptide having a cyclic structure or a pharmaceutically acceptable salt thereof according to claim 4, wherein  $X^p$  ( $n_p=1$ ) is  $X^8$  and  $X^q$  ( $n_q=1$ ) is  $X^{14}$ .

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12. A peptide having a cyclic structure or a pharmaceutically acceptable salt thereof according to claim 5, wherein  $X^p$  ( $n_p=1$ ) is  $X^3$  and  $X^q$  ( $n_q=1$ ) is a C-terminal residue.

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13. A peptide having a cyclic structure or a pharmaceutically acceptable salt thereof according to claim 4, wherein  $X^p$  ( $n_p=1$ ) is  $X^3$  and  $X^q$  ( $n_q=1$ ) is not a C-terminal residue.

14. A peptide having a cyclic structure or a pharmaceutically acceptable salt thereof according to claim 6, wherein  $X^p$  ( $n_p=1$ ) is an N-terminal residue and  $X^q$  ( $n_q=1$ ) is  $X^{11}$ .

5  
15. A peptide having a cyclic structure or a pharmaceutically acceptable salt thereof according to claim 1, said peptide having an amino acid sequence shown by one of SEQ ID NOS: 4-7 and 16-32 in which one to several residues which  
10 are the same or different and arbitrarily selected from the group consisting of organic acid residue, amino acid residues and a 12-aminododecanoic acid residue mentioned in the  $X^i$  representations in claim 1 may be deleted, substituted or added.

15  
16. A peptide having a cyclic structure or a pharmaceutically acceptable salt thereof according to claim 15, said peptide having an amino acid sequence shown by one of SEQ ID NOS: 4-7, 16, 19 and 25-32 in which one to several  
20 residues which are the same or different and arbitrarily selected from the group consisting of organic acid residues, amino acid residues and a 12-aminododecanoic acid residue mentioned in the  $X^i$  representations in claim 1 may be deleted, substituted or added.